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Typed or Printed Name		Fedelina TORRES	
Signature		Date	June 19, 2002

<b>Supplemental Amendment</b>  Address to: Assistant Commissioner for Patents Washington, D.C. 20231	Application Number	09/398,399
	Attorney Docket Number	10981620-2
	Filing Date	September 17, 1999
	First Named Inventor	Delenstarr
	Examiner	Sisson, B.
	Group Art	1655
	Title	Techniques for Assessing Nonspecific Binding of Nucleic Acids to Surfaces

Sir:

In view of the amendments to the claims and the remarks put forth below, reconsideration and allowance are respectfully requested.

AMENDMENTS

In the title:

Please amend the title to read:

**ARRAYS COMPRISING BACKGROUND FEATURES THAT PROVIDE FOR A MEASURE OF NON-SPECIFIC BINDING AND METHODS FOR USING THE SAME**

In the claims:

50. (Amended) A hybridization assay comprising:

(a) contacting a sample of target nucleic acids under hybridization conditions where a target nucleic acid of 14 nucleotides in length must have no less than 70% sequence identity with a probe in order to hybridize to said probe with a collection of substrate bound probe nucleic acid features that includes at least one background nucleic acid feature that is an empirically observed inactive probe that does not hybridize to its fully complementary target as determined in an assay wherein said probe is provided in an array that is contacted with said fluorescently labeled fully complementary target under said hybridization conditions; and

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cont. (b) detecting the presence of target nucleic acids hybridized to said collection of probe nucleic acid features.

58. (Amended) A hybridization assay comprising:

G2 (a) contacting a sample of target nucleic acids under hybridization conditions where a target nucleic acid of 14 nucleotides in length must have no less than 70% sequence identity with a probe in order to hybridize to said probe with a collection of substrate bound probe nucleic acid features that includes at least one background nucleic acid feature, wherein said at least one background feature is made up of a probe nucleic acid selected from the group consisting of SEQ ID NOS: 05 to 32; and

(b) detecting the presence of target nucleic acids hybridized to said collection of probe nucleic acid features.

59. (Amended) A hybridization assay comprising:

(a) contacting a sample of target nucleic acids under hybridization conditions where a target nucleic acid of 14 nucleotides in length must have no less than 70% sequence identity with a probe in order to hybridize to said probe with a collection of substrate bound probe nucleic acid features that includes at least one background nucleic acid feature, wherein said at least one background feature is made up of a probe nucleic acid that is chosen from:

(i) a probe nucleic acid that forms a stable intramolecular structure; (ii) a probe nucleic acid that comprises reverse polarity nucleotide analogs; and (iii) a probe nucleic acid that comprises abasic phosphodiester; and

(b) detecting the presence of target nucleic acids hybridized to said collection of probe nucleic acid features.

60. (Amended) A hybridization assay comprising:

(a) contacting a sample of detectably labeled target nucleic acids under hybridization conditions where a target nucleic acid of 14 nucleotides in length must have no less than 70% sequence identity with a probe in order to hybridize to said probe with an array of probe nucleic acid features that includes at least one background nucleic acid feature that is an empirically observed inactive probe that does not hybridize to its fully complementary target as determined in an assay wherein said probe is provided in an array that is contacted with said fluorescently labeled fully complementary target under said

hybridization conditions;

62. (b) separating non-hybridized target nucleic acids from said array; and  
(c) detecting the presence of target nucleic acids hybridized to said array probe

nucleic acid features.

62. (Amended) A hybridization assay comprising:

63. (a) contacting a sample of detectably labeled target nucleic acids conditions where a target nucleic acid of 14 nucleotides in length must have no less than 70% sequence identity with a probe in order to hybridize to said probe with an array of probe nucleic acid features that includes at least one background nucleic acid feature, wherein said at least one background feature is made up of a probe nucleic acid selected from the group consisting of SEQ ID NOS: 05 to 32;

- (b) separating non-hybridized target nucleic acids from said array; and  
(c) detecting the presence of target nucleic acids hybridized to said array probe nucleic acid features.

63. (Amended) A hybridization assay comprising:

(a) contacting a sample of detectably labeled target nucleic acids conditions where a target nucleic acid of 14 nucleotides in length must have no less than 70% sequence identity with a probe in order to hybridize to said probe with an array of probe nucleic acid features that includes at least one background nucleic acid feature, wherein said at least one background feature is made up of a probe nucleic acid that is chosen from: (i) a probe nucleic acid that forms a stable intramolecular structure; (ii) a probe nucleic acid that comprises reverse polarity nucleotide analogs; and (iii) a probe nucleic acid that comprises abasic phosphodiester;

- (b) separating non-hybridized target nucleic acids from said array; and  
(c) detecting the presence of target nucleic acids hybridized to said array probe nucleic acid features.

64. (Amended) A hybridization assay comprising:

(a) contacting a sample of target nucleic acids under hybridization conditions where a target nucleic acid of 14 nucleotides in length must have no less than 70% sequence identity with a probe in order to hybridize to said probe with an array of probe nucleic acid

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features that includes at least one background nucleic acid feature that is an empirically observed inactive probe that does not hybridize to its fully complementary target as determined in an assay wherein said probe is provided in an array that is contacted with said fluorescently labeled fully complementary target under said hybridization conditions;

- (b) separating non-hybridized target nucleic acids from said array;
  - (c) detectably labeling target nucleic acids hybridized to said array of probe nucleic acid features; and
  - (d) detecting the presence of target nucleic acids hybridized to said array of probe nucleic acid features.
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66. (Amended) A hybridization assay comprising:

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where a target nucleic acid of 14 nucleotides in length must have no less than 70% sequence identity with a probe in order to hybridize to said probe with an array of probe nucleic acid features that includes at least one background nucleic acid feature, wherein said at least one background feature is made up of a probe nucleic acid selected from the group consisting of SEQ ID NOS: 05 to 32;

- (b) separating non-hybridized target nucleic acids from said array;
- (c) detectably labeling target nucleic acids hybridized to said array of probe nucleic acid features; and
- (d) detecting the presence of target nucleic acids hybridized to said array of probe nucleic acid features.

67. (Amended) A hybridization assay comprising:

(a) contacting a sample of target nucleic acids under hybridization conditions where a target nucleic acid of 14 nucleotides in length must have no less than 70% sequence identity with a probe in order to hybridize to said probe with an array of probe nucleic acid features that includes at least one background nucleic acid feature, wherein said at least one background feature is made up of a probe nucleic acid that is chosen from: (i) a probe nucleic acid that forms a stable intramolecular structure; (ii) a probe nucleic acid that comprises reverse polarity nucleotide analogs; and (iii) a probe nucleic acid that comprises abasic phosphodiester;

- (b) separating non-hybridized target nucleic acids from said array;

(c) detectably labeling target nucleic acids hybridized to said array of probe nucleic acid features; and

(d) detecting the presence of target nucleic acids hybridized to said array of probe nucleic acid features.

68. (Amended) A kit for use in a hybridization assay, said kit comprising:  
a collection of substrate bound probe nucleic acid features that includes at least one background nucleic acid feature that is made up of a probe nucleic acid selected from the group consisting of SEQ ID NOS: 05 to 32.

Cancel Claims ~~69~~ and ~~70~~.

71. (Amended) A hybridization assay comprising:

(a) contacting a sample of target nucleic acids under hybridization conditions where a target nucleic acid of 14 nucleotides in length must have no less than 70% sequence identity with a probe in order to hybridize to said probe with a collection of substrate bound probe nucleic acid features that includes at least one background nucleic acid feature made up of background probes that do not selectively bind to any of said target nucleic acids; and

(b) detecting the presence of target nucleic acids hybridized to said collection of probe nucleic acid features.

Please add the following new claims:

--79. (New) The method according to Claim 59, wherein said stable intramolecular structure is a hairpin.

80. (New) The method according to Claim 59, wherein said stable intramolecular structure is a pseudo-half knot.

81. (New) The method according to Claim 63, wherein said stable intramolecular structure is a hairpin.

82. (New) The method according to Claim 63, wherein said stable intramolecular

structure is a pseudo-half knot.

83. (New) The method according to Claim 67, wherein said stable intramolecular structure is a hairpin.

84. (New) The method according to Claim 67, wherein said stable intramolecular structure is a pseudo-half knot.--

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### REMARKS

In view of the above amendments and the following remarks, the Examiner is respectfully requested to withdraw all of the remaining rejections and allow Claims 50-68 and 71-78, as well as newly presented Claims 79-84, the only claims pending and currently under examination in this application.

### Amendments

All of the independent claims have been amended to clarify the language used in the claims to describe the hybridization conditions.

In addition, Claims 50, 60 and 64, which are directed to background probes that are empirically determined inactive probes as discussed in the specification and exemplified in Examples 1 and 2, have been amended to replace the language: "minimally binds to its complementary target under said hybridization conditions" with the language: "is an empirically observed inactive probe that does not hybridize to its fully complementary target as determined in an assay wherein said probe is provided in an array that is contacted with said fluorescently labeled fully complementary target under said hybridization conditions." This amendatory language finds full support in Example 1, where a candidate probe on an array is contacted with a fluorescently labeled target that is its full complement.

Furthermore, Claims 59, 63 and 67 have been amended to replace the phrase "minimally binds to an R6G-labeled yeast cRNA target pool according to the test assay described in Example 3.B." with the phrase "is chosen from: (i) a probe nucleic acid that forms a stable intramolecular structure that is one of a hairpin and a pseudo-half knot; (ii) a

probe nucleic acid that comprises reverse polarity nucleotide analogs; and (iii) a probe nucleic acid that comprises abasic phosphodiester." Support for this new language is clearly found in the specification at page 22, lines 1 to 5 and in the working exemplification.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE.**" Applicants respectfully request reconsideration of the application in view of the amendments and remarks made herein.

### **Rejections**

The remaining issues with the claims are summarized in the Examiner's interview. With respect to the first issue concerning the hybridization conditions, the language in the claims has been clarified in accordance with that which was discussed and agreed to by the Examiner during the interview.

With respect to the term "minimally" in the claims, this term has been removed from the claim language.

With respect to the language concerning Example 3B in the claims, this language has been replaced with method steps taken from the Examples, consistent with the Examiner's suggestion.

With respect to the kit claims, it is believed that the above amendments make these claims allowable.

Finally, the title of the application has been amended pursuant to the Examiner's suggestion.

### **Conclusion**

The applicant respectfully submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference

would expedite the prosecution of this application, please telephone Gordon Stewart at 650 485 2386. The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-1078.

Respectfully submitted,

Date: June 19, 2002

By: 

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